# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

| | | |
|---|---|---|
| Applicant's or agent's file reference<br>O07F1496 | **FOR FURTHER ACTION** | See item 4 below |
| International application No.<br>PCT/JP2004/014941 | International filing date *(day/month/year)*<br>08 October 2004 (08.10.2004) | Priority date *(day/month/year)*<br>10 October 2003 (10.10.2003) |
| International Patent Classification (8th edition unless older edition indicated)<br>See relevant information in Form PCT/ISA/237 | | |
| Applicant<br>ONO PHARMACEUTICAL CO., LTD. | | |

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

| | | |
|---|---|---|
| ☒ | Box No. I | Basis of the report |
| ☐ | Box No. II | Priority |
| ☒ | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| ☒ | Box No. IV | Lack of unity of invention |
| ☒ | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| ☒ | Box No. VI | Certain documents cited |
| ☐ | Box No. VII | Certain defects in the international application |
| ☒ | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

| | |
|---|---|
| | Date of issuance of this report<br>20 June 2006 (20.06.2006) |
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland | Authorized officer<br>Yoshiko Kuwahara |
| Facsimile No. +41 22 740 14 35 | Telephone No. +41 22 338 90 90 |

Form PCT/IB/373 (January 2004)

# PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

# PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

| | |
|---|---|
| | Date of mailing *(day/month/year)* |
| Applicant's or agent's file reference<br>007F1496 | FOR FURTHER ACTION<br>See paragraph 2 below |

| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
|---|---|---|
| PCT/JP2004/014941 | 08.10.2004 | 10.10.2003 |

International Patent Classification (IPC) or both national classification and IPC

Applicant
ONO PHARMACEUTICAL CO., LTD.

1. This opinion contains indications relating to the following items:

| | | |
|---|---|---|
| ☒ | Box No. I | Basis of the opinion |
| ☐ | Box No. II | Priority |
| ☒ | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| ☒ | Box No. IV | Lack of unity of invention |
| ☒ | Box No. V | Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| ☒ | Box No. VI | Certain documents cited |
| ☐ | Box No. VII | Certain defects in the international application |
| ☒ | Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

| | |
|---|---|
| Name and mailing address of the ISA/JP<br><br>Facsimile No. | Authorized officer<br><br>Telephone No. |

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/014941

**Box No. I** Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/014941

**Box No. III** **Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 4, 20, 21

because:

☒ the said international application, or the said claims Nos. 20, 21
relate to the following subject matter which does not require an international preliminary examination (*specify*):

The subject matters of claims 20 and 21 relate to a method for treatment and diagnosis of the human body by surgery or therapy.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☒ the claims, or said claims Nos. 4 are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 4, 20, 21

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/014941

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:

   ☐ paid additional fees

   ☐ paid additional fees under protest

   ☐ not paid additional fees

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

While the subjects common to the inventions relevant to claims 1-19, 22 and 23 are chemical compounds comprising a condensed hetero-cycle structure described in page 8-10, such structures have been long known as basic structures of a condensed hetero-cycle compound, and obviously does not appear to be novel as shown in documents 1-4 hereinafter.

As a result, these common subjects are not considered to be of special technical features in the meaning of paragraph 2 of the PCT rule 13.2. Also, there being no common subject considered to have other special technical features, it is not possible to find any technical relevance in the meaning of the PCT rule 13 among the different inventions. Therefore, the inventions relevant to claims 2-19, 22 and 23 do not meet the requirement of unity of invention.

4. Consequently, this opinion has been established in respect of the following parts of the international application:

   ☐ all parts

   ☒ the parts relating to claims Nos. 1-3, 5-19, 22, 23

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/014941

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 3, 6, 7, 13 | YES |
| | Claims | 1, 2, 5, 8-12, 14-19, 22, 23 | NO |
| Inventive step (IS) | Claims | 3, 6, 7, 13 | YES |
| | Claims | 1, 2, 5, 8-12, 14-19, 22, 23 | NO |
| Industrial applicability (IA) | Claims | 1-3, 5-19, 22, 23 | YES |
| | Claims | | NO |

2. Citations and explanations:

Document 1: WO, 2002/083648, A1, working example I-173
Document 2: Darren Krause et al., 'Transient activation of June N-terminal kinases and protection from apoptosis by the insulin-like growth factor I receptor can be suppressed by dicumarol.', J Biol Chem. Jun 1, 2001 (01.06.01), Vol. 276, No.22, pp. 19244-19252
Document 3: WO, 2000/064872, A1
Document 4: WO, 2003/059900, A1

Claims 1, 2, 8-11, 14-16, 18, 19 and 22 are described in document 1 referred to in the ISR, and therefore, do not appear to be novel and to involve an inventive step. Since claim 2 relates to a compound having benzo-pyran structure and having a JNK inhibitory behavior, those suitable for the use of therapeutic agents for chronic articluar rheumatisms and diabetes are shown in working examples I-173.

Claims 1, 2, 8-10, 14 and 22 are described in document 2 referred to in the ISR, and do not appear to be novel or to involve an inventive step. Document 2 describes dicumarol as a JNK inhibitory agent.

Claims 1, 2, 8-10, 14-19 and 22 are described in document 3 referred to in the ISR and do not appear to be novel and to involve an inventive step. The compound having benzo-pyran structure described in document 2 are described in working example 170 or 175, and it is described in page 108-109 thereof that the said compound is suited for the use of therapeutic agents for inflammatory diseases and diabetes. Also, claim 23 does not appear to involve an inventive step as these are indicated to use together with other agents in page 116-117 of document 3.

Claims 1, 2, 5, 8, 12 and 23 are described in document 4 referred to in the ISR and do not appear to be novel and to involve an inventive step. The working example of document 4 (for reference) describes various types of chromen compounds and further describes that document 17 and others describe that these are used in combination with HMG-CoA reducing enzyme inhibitory agents.

The group of compounds described in claims 3, 6, 7 and 13 and those JNK inhibitory effects are neither described nor indicated in above claims 1-4.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/014941

**Box No. VI** **Certain documents cited**

1. Certain published documents (Rule 43*bis*.1 and 70.10)

| Application No. Patent No. | Publication date (day/*month*/year) | Filing date (day/*month*/year) | Priority date (valid claim) (*day*/month/*year*) |
|---|---|---|---|
| WO 2004/081013 A1 [P, X] | 23.09.2004 | 11.03.2004 | 11.03.2003 |
| WO 2004/076458 A1 [P, X] | 10.09.2004 | 01.03.2004 | 28.02.2003 |
| WO 2004/087707 A1 [P, X] | 14.10.2004 | 18.03.2004 | 31.03.2003 |
| US 2004/209878 A1 [P, X] | 21.10.2004 | 11.02.2004 | 04.09.2002 |
| WO 2004/026229 A1 [P, X] | 01.04.2004 | 03.09.2003 | 04.09.2002 |

2. Non-written disclosures (Rule 43*bis*.1 and 70.9)

| Kind of non-written disclosure | Date of non-written disclosure (day/*month*/year) | Date of written disclosure referring to non-written disclosure (*day*/month/*year*) |
|---|---|---|

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/014941

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

In connection with claims 1-3, 5, 8-12, 14-19, 22 and 23 which relate to inventions of the compounds comprising a wide range of compounds themselves, those usage and the composition, since the group of compounds corresponding to the general formula I-2 are not fully supported in the description as described in claim 4, the compounds with a quinazoline structure among the said claims has been set aside from the search objects.
Also, regarding the compounds with other structure, since those supported in the description in the meaning of PCT rule 6 and those disclosed in the meaning of PCT rule 5 are only the compounds of which substituent R2 is bonded through nitrogen atoms, search has been made focusing on the compounds of which substituent R2 is bonded through nitrogen atoms among general formula of I-1 or I-3.

Further, a complete search has been made on claims 7 and 13.

In connection with the medical use of claims 14-19 and 23, any specific data indicating the said medical effectiveness is not shown and is not supported fully in the description. Especially, it could not be understood by a person skilled in the art that all the wide range of compounds described in these claims are effective to the said medical use.